Center for Dermal Research
Innovations in Dermatological Sciences Conference 2023

Dr. Kevin Mills

Dr. Kevin Mills is a recently retired R&D Director Principal Scientist with P&G Global Bioscience in Cincinnati, Ohio, where he led a team that applies contemporary methods in cell and molecular biology to physiologically define skin health and to discover new materials to improve skin condition by targeting pathways that regulate epidermal homeostasis and circadian rhythms.

Dr. Mills joined P&G in 1994 and held positions focused on various aspects of skin biology, ranging from human safety to skin barrier function, epidermal homeostasis, and inflammation. His teams have developed in vitro and ex vivo models to simulate inflammatory cascades important in a wide variety of epithelial inflammatory disorders, which has led to the identification of gene expression signatures useful in the identification of new cutaneous therapeutics. More recently, his team has discovered that human skin is a window into systemic circadian phase and can be sampled to determine the relationship between a person's body time and wall clock time. This skin circadian oscillator can be used by clinicians to determine the best time to administer a drug or time a medical procedure.

Dr. Mills graduated from Stony Brook University with a B.S. in Biological Sciences, and obtained the M.S. and Ph.D. degrees in Toxicology, from North Carolina State University, where he studied molecular mechanisms of chemical carcinogenesis in the skin. Dr. Mills completed post-doctoral training at the National Institute of Environmental Health Sciences (NIH), where he studied the regulation by retinoids of the differentiation of the skin and other epithelia. He is now a Visiting Scientist in the Department of Biological Sciences at North Carolina State University.

"Characterization of the Biological Activity of a Unique Botanical Extract to Treat Atopic Dermatitis"

Abstract:

Atopic dermatitis (AD) is a chronic inflammatory skin disease that affects 15-20% of children and 1-3% of adults worldwide. First-line therapies such as corticosteroids effectively reduce disease flares but have significant side effects. The purpose of these studies was to evaluate a natural extract (BW22) and BW22 plus a colloidal oatmeal (CO) extract as potential topical

therapies for AD. BW22 is a unique mixture of extracts derived from 22 plant species known to contain biologically active compounds. To simulate AD inflammation, primary normal human keratinocytes were treated for 24 hours with a combination of IL-4, IL-13, IL-22, and IFN-g, a stimulus known to evoke AD-like cascades of gene expression (AD stimulus). Co-administration of BW22 or BW22 + CO with this stimulus resulted in dose-dependent suppression of the release of CCL-5 into the growth medium. Maximal suppression of CCL-5 approached 100%, exceeding that seen with clobetasol propionate (CP; 5 mM), a potent topical corticosteroid. To gain mechanistic insight into BW22 and BW22 + CO, we performed microarray analysis. Using two independent computational techniques (unbiased clustering and gene set enrichment) we found that both BW22 and BW22 + CO strongly prevented the induction of genes by the AD stimulus; these included genes with GO terms of cytokine mediated pathways, interferon signaling, innate immunity and defense response. In addition, BW22 and BW22 + CO prevented the repression of genes by the AD stimulus, most notably those associated with cell adhesion. Together, this prevention suggests the potential of BW22 + CO to rescue skin homeostasis. Comparisons of BW22+CO with CP indicated BW22+CO produced a more robust dampening of inflammatory response genes while also inducing genes involved in skin development and barrier function. CP either repressed these genes or had no effect. Finally, after integrating findings from two different computational tools (Ingenuity Pathway Analysis and Connectivity Mapping) we determined BW22+ CO is strongly associated with and likely functions through an interconnected mechanism involving EphrinA activation, EGFR repression and both AHR and NRF-2 induction, leading to diminished inflammation and restoration of epidermal homeostasis. Collectively, these data support that BW22+ CO is a potent non-steroidal anti-inflammatory capable of restoring keratinocyte homeostasis and repressing both innate and adaptive immune responses associated with AD.